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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,683	07/19/2002	James S. Nowick	UCIVN-001US	3685

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EXAMINER	
LUKTON, DAVID	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 08/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,683	NOWICK ET AL.	
	Examiner	Art Unit	
	David Lukton	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *2-9 and 12-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,10 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Pursuant to the directives of the response filed 5/31/05, claims 1, 10 and 11 have been amended. Claims 1, 10 and 11 are examined in this Office action; claims 2-9, 12-31 remain withdrawn from consideration.

✦

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 10, 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are now drawn to a composition of matter that "comprises" the compound of claim 1 (for which a structural formula is provided). However, there does not appear to be support for use of the term "comprises" in this situation. For example, on page 4, lines 3-4, the following is recited:

"These compositions [of matter] have the general formula A"

This is not consistent with the term "comprising" to describe the genus of compounds.

It is also noted that the term "incorporated into" is used on page 5 of the specification. However, (a) "incorporated into" is not the same as comprising, and (b) where the "incorporated into" language is used, it is referring to one of a few specific situations, and does not provide support for any and all compounds that "comprise" the structure provided in claim 1.

Descriptive support for the claimed invention is thus lacking. It is suggested that the first two lines of text (of claim 1) be deleted and replaced with the following:

-- A compound of the formula --

✧

Claims 1, 10, 11 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants have determined (fig 7) the NMR chemical shifts of the *alpha*-protons of Phe and Val in "tripeptide A" as a function of concentration (of "tripeptide A") in $CDCl_3$. Applicants have also asserted (page 12, line 1) that in 10% $CD_3OD/CDCL_3$, dimerization of tripeptide A occurs with a K_{dim} of 900 M^{-1}. Applicants have also proposed various structural models. Such models may, at some point in the future, prove to be relevant to the actual structures present in solution. But as matters

currently stand, all that applicants have provided evidence for is the proposition that tripeptide A can dimerize in chloroform, or in chloroform containing 10% methanol.

Applicants have asserted (page 5, line 4+) that if the compounds of claim 1 are incorporated into peptides, such proteins will dimerize by means of beta-sheet interactions. Also asserted (page 5, line 12+) is that if one of the claimed compounds is "incorporated into a drug or agent", it will block the beta-sheet dimerization of proteins. First, applicants have not actually shown that there exists two proteins which dimerize in the absence of the claimed compounds, but will not dimerize in the presence of any of the claimed compounds. Nor have applicants even shown that any of the claimed compounds can dimerize in aqueous solution. Further, there is no guidance as to which peptides one should incorporate the claimed compounds into, or which proteins they might possibly inhibit the dimerization of. As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims. Thus, there are no working examples which show one how to inhibit dimerization of proteins, and no guidance as to

which peptides one should incorporate the claimed compounds into, or which proteins they will inhibit the dimerization of. Nor is there any guidance provided by the prior art which can be applied to the claimed compounds. In addition, one cannot predict, merely by viewing a structure, which compounds will inhibit dimerization of a given pair of proteins. In accordance with the foregoing, "undue experimentation" would be required to practice the claimed invention.

In response to the foregoing, applicants have begun by arguing that the elected claims are drawn to compositions of matter, and not to methods. This particular point is correct; however, the specification must still show the skilled artisan "how to use" the claimed compositions of matter. Next, applicants have argued that the specification provides a description of what each claimed composition of matter "is". What this particular statement might mean is not made clear. But in any case, the issue is whether or not the specification teaches the skilled artisan how to use the claimed compositions of matter. The examiner maintains that it does not. Applicants have also argued that the specification describes how to make the claimed compositions of matter. The examiner will stipulate that the skilled artisan could synthesize any one of the compounds to which the claims are drawn, but the examiner has not previously (or currently) made any assertion to the contrary. Next, applicants have argued that the specification has offered various assertions about how a person might try to use the

compounds at some point in the future. The examiner will concede that the specification does offer some speculation in this regard. However, the specification does not show the skilled artisan how to use the claimed compositions of matter to inhibit dimerization of a given pair of proteins. Next, applicants have "called to the examiner's attention" to U.S. Patents 5,618,914 and 6,020,331. Applicants have not explained the relevance. But perhaps it is applicants opinion that somewhere in the disclosure of the '914 or '331 patents, there is evidence that a compound can inhibit dimerization of a given pair of proteins. If applicants believe this to be the case, applicants should point out the relevant column and line numbers where such evidence is presented. Probably applicants will not be able to do this, but even if such evidence has been presented in these patents, it will have little bearing in the instant case. Perhaps it is true that another chemist has been able to show that a compound unrelated to the claimed invention is effective to inhibit dimerization of a given pair of proteins. If true, this will not provide enablement for the claimed compositions of matter. As it happens, structure/activity relationships are "unpredictable"; minor changes in structure can eliminate the inhibitory capability of a given compound. Then there is the matter of which proteins are susceptible to a given inhibitor. The specification provides no guidance in this regard.

Thus, apart from some vague speculation, the specification provides no guidance as to

how to use the claimed compositions of matter, or which proteins they will inhibit the dimerization of. There are no working examples which show this either. Nor does the prior art provide any suggestion that the claimed compositions of matter can inhibit dimerization of proteins. And the field of protein biochemistry is very unpredictable; one cannot extrapolate from the effects of one compound on the dimerization of a given pair of proteins to any particular effect of another compound on the dimerization of some other set of proteins.

It is maintained that "undue experimentation" would be required to practice the claimed invention.

✦

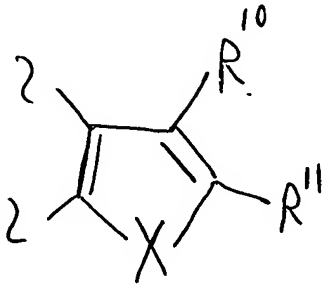
Claims 1, 10, 11 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- The definition of "W", in conjunction with the indicated structure, generates an ambiguity in claim 1. The claim recites the following:

  "W is hydrogen or fluorine or **the** NHCOCOZ group shown".

  It is unclear what exactly is meant by "**the** NHCOCOZ group shown". One interpretation is that when "W" is other than hydrogen or fluorine, then "W" must be NHCOCOZ, and at the same time the adjacent position on the ring must be hydrogen. Another interpretation is that when "W" is other than hydrogen or fluorine, then "W" must be NHCOCOZ, and at the same time the adjacent position on the ring can also

be NHCOCOZ. Which of these is intended? One option for enhancing clarity would be to define two new variables, e.g., R^{10} and R^{11}, and to provide the following structure (only a partial structure is shown here for simplicity):



These two variables could then be defined as follows:

R^{10} is hydrogen or fluorine or NH-CO-CO-Z;

R^{11} is hydrogen or NH-CO-CO-Z;
with the proviso that one of R^{10} and R^{11} is NH-CO-CO-Z.

- Claim 1 recites that variable "X" can represent $-N=CR^4$. However, this requires the carbon atom bearing R^4 to be trivalent. If applicants believe that this structural formula is correct, applicants are requested to provide an example of a specific compound that corresponds to this possibility for "X".

- Claim 1 recites that R^2 can be an acyclic aryl, or an unbranched, chiral alkyl group. Applicants are requested to provide an example of each of these. The same issue applies in the case of variables R^1, R^6, R^7 and R^8.

- Claim 11 is drawn to a compound that comprises $(Me)_2CHCO$-Phe-Hao-Val-NHBu. Claim 11 is recited to be dependent on claim 1. While it may be true that claim 1 would encompass the possibility of a "composition of matter" which has the structure in question, or comprises it, claim 1 does not encompass the possibility of a compound comprising the structure in question. Accordingly, claim 11 is not properly subgenric

to claim 1. One option is to recast claim 11 in independent form.

✦

The following is a quotation of the appropriate paragraphs of 35 U.S.C 102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

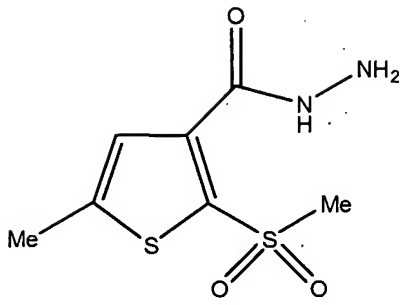
(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

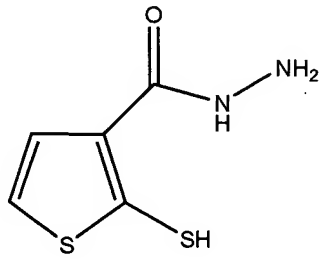
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 1 is rejected under 35 U.S.C. §102(b) as being anticipated by Krayushkin (*Isvestiya Akademii Nauk, Seriya Khimicheskaya* 1, 114-117, 1994)

Krayushkin discloses compound 4a, which has the following structure:



Claim 1 is drawn to a composition of matter that "comprises" a compound. One of the compounds encompassed by instant claim 1 is the following:



Because of the "comprising" language in claim 1, this claim encompasses not only the second structure shown (above), but the first one as well.

Thus, the claim is anticipated.

✦

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at (571)272-0974. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

DAVID LUKTON
PATENT EXAMINER
GROUP 1800